Ring Expansion of 4-Alkynylcyclobutenones. Synthesis of Piperidinoquinones, Highly Substituted Dihydrophenanthridines, Benzophenanthridines, and the Naturally Occurring Pyrrolophenanthridine, Assoanine

Yifeng Xiong and Harold W. Moore*

Department of Chemistry, University of California−Irvine, Irvine, California 92717

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New synthetic routes to a variety of N-heterocyclic quinones and hydroquinones are described. These include thermolyses of 4-hydroxy-4-[4-*N*-(benzenesulfonyl)-4-aza-1,6-dialkynyl]cyclobutenones to piperidinoquinones and 4-hydroxy-4-[3-(*N*-phenylamino)-1-propynyl]cyclobutenones to dihydrophenanthridinediols. Included in the array of products available by this method are benzophenanthridines, indolophenanthridines, isoindoloindoles, and pyrrolophenanthridines. The methodology was employed in a five-step synthesis of the alkaloid assoanine starting with dimethyl squarate and indoline. The key step in all of these transformations is the ring expansion of appropriately substituted 4-hydroxy-4-alkynylcyclobutenones. These are envisaged to undergo electrocyclic ring opening to the corresponding enynylketenes which ring close to diradical intermediates that then lead to products via either radical additions to proximal alkyne moieties or undergo homolytic aromatic substitution to appropriately placed aryl groups. The synthetic scope and mechanism of the ring expansion reactions are discussed.

Introduction and Overview

Reported here is a highly convergent route to a variety of N-heterocyclic ring systems, including piperidinoquinones, benzophenanthridines, indolophenanthridines, isoindoloindoles, and pyrrolophenanthridines. The method entails the thermal rearrangements of selected 4-hydroxy-4-[4-*N*-(benzenesulfonyl)-4-aza-1,6-alkadiynyl]cyclobutenones and 4-hydroxy-4-(4-*N*-aryl-4-aza-1,6-alkadiynyl)cyclobutenones to piperidinoquinones **17** (Scheme 3) and highly substituted phenanthridines **22** (Scheme 4), respectively**.** Although rare, the piperidinoquinone skeleton is found as a subunit in naturally occurring N-heterocyclic quinones such as the cyanocycline and saframycin families.[1,2] In contrast, phenanthridines are quite common, but available methods are limited for regiospecific syntheses of highly substituted derivatives. This is particularly true for heterocyclic quinones in this series. That drawback is circumvented by the method outlined here which allows construction of highly condensed polycyclic analogs from readily available starting materials. Particularly noteworthy is the utility of these ring expansions as key steps in the synthesis the **39** (Scheme 9) and **43** (Scheme 10). The former is an example of the ring system found in the benzophenanthridine alkaloid family. The latter is an intermediate in the synthesis of assoanine (**40**), a naturally occurring pyrrolophenanthridine.

The synthetic methodology presented here stems from the thermal rearrangement of 4-alkynyl-4-hydroxycyclobutenones, a reaction that is envisaged to lead to products via a mechanism involving the formation of enynylketenes and diradical intermediates. Although a number of applications of this rearrangement have been reported, its scope and limitations are still incompletely defined.[3−6] Selected previously reported examples that directly relate to the syntheses described herein are given in Scheme 1. Specifically, thermolysis of 4-(1,5-dialkynyl)-4-hydroxycyclobutenones **1** was shown to give carbocyclic annulated quinones **5**.[4] This is considered to involve initial electrocyclic ring opening of **1** to enynylketene **2** followed by subsequent ring closure to diradical **3**. The more reactive ring-based radical center in **3** then adds to the proximal alkyne group to give **4** which undergoes intramolecular H-atom abstraction from the neighboring hydroxyl group to provide the annulated quinone **5**. In an analogous reaction, aryl radical additions to alkene groups were realized as evidenced by the formation of pyranoquinones from the corresponding 4-enynylcyclobutenones, e.g., **6** → **7**.[3] Finally, it is noted that arylations involving intermediates generally represented by diradical **8** have also been reported.[5] Additional examples of the above reaction types as they apply to the syntheses of selected N-heterocyclic systems are provided below.

Synthesis of Piperidinoquinones

Synthesis of piperidinoquinones, as described here, depends upon the availability of the previously unknown 4-hydroxy-4-[4-*N*-(benzenesulfonyl)-4-aza-1,6-alkadiynyl]-cyclobutenolnes **14** (Scheme 3). These are now available as outlined here and araise from 4-aza-1,6-diynes which were prepared by two methods (Scheme 2). The first

[⊗] Abstract published in *Advance ACS Abstracts,* December 15, 1996.

(1) Thomson, R. H. *Naturally Occurring Quinones III--Recent Advances*; Chapman Hall: London, New York, 1987; pp 633−666.

(2) (a) Park, A.; Schmitz, F. J. *Tetrahedron Lett.* **1993**, *34,* 3983. (b) Davidson, B. S. *Tetrahedron Lett.* **1992**, *33*, 3721. (c) McKee, T. C.; Ireland, C. M. *J. Nat. Prod.* **1987**, *50*, 754. (d) McKillop, A.; Brown, S. P. *Syn. Commun.* **1987**, *17(6),* 657. (e) Kobayashi, M.; Rao, S. R.; Chavakula, R.; Sarma, N. S. *J. Chem. Res. (S)* **1994**, 282.

(3) Xiong, Y., Moore, H. W. *J. Org. Chem.* **1995**, *60*, 6460.

(4) Xia, H.; Moore, H. W. *J. Org. Chem.* **1992**, *57*, 3765.

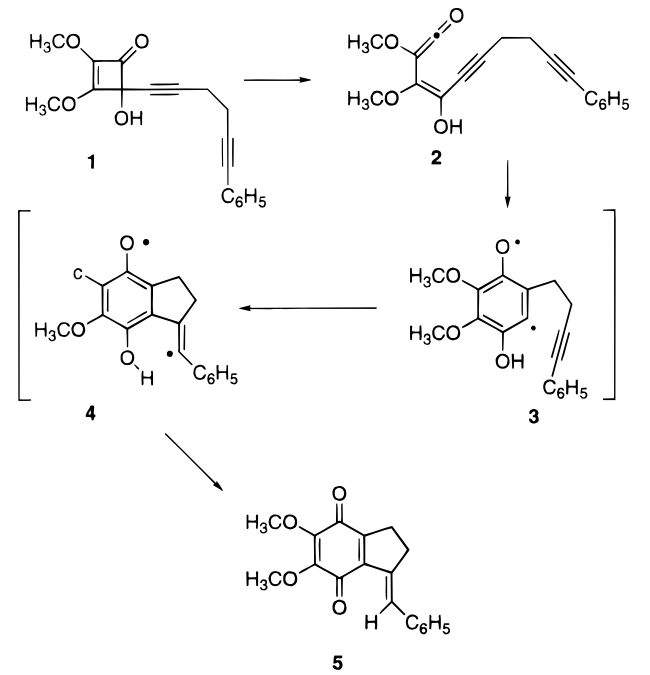
(5) For a recent review on the synthetic utility of cyclobutenones see: Moore, H. W.; Yerxa, B. R. *Adv. Strain Org. Chem.* **1995**, *4*, 81−162.

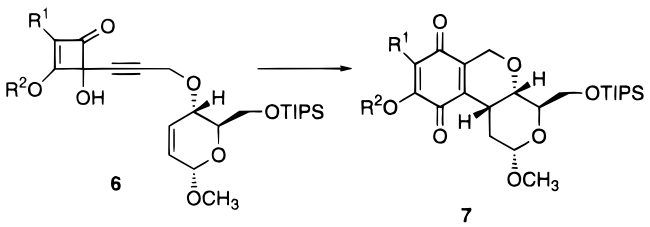
(6) For an excellent review on the generation of diradicals from enediynes, enynylallenes, and enynylketenes see: (a) Wang, K. W. *Chem. Rev.* **1996**, *96*, 207. (b) Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453.

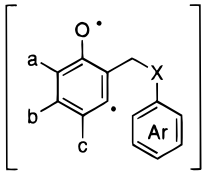
(7) Padwa, A.; Nimmesgern, H.; Wong, G. S. K. *J. Org. Chem.* **1985**, *50*, 5620.

S0022-3263(96)01380-1 CCC: $12.00

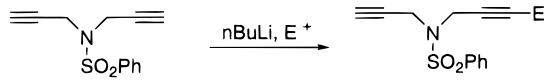
Scheme 1





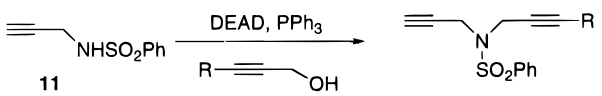


Scheme 2



9

10a E = TMS, 50%
10b E = $(CH_3)_2COH$, 62%
10c E = PhCHOH, 49%



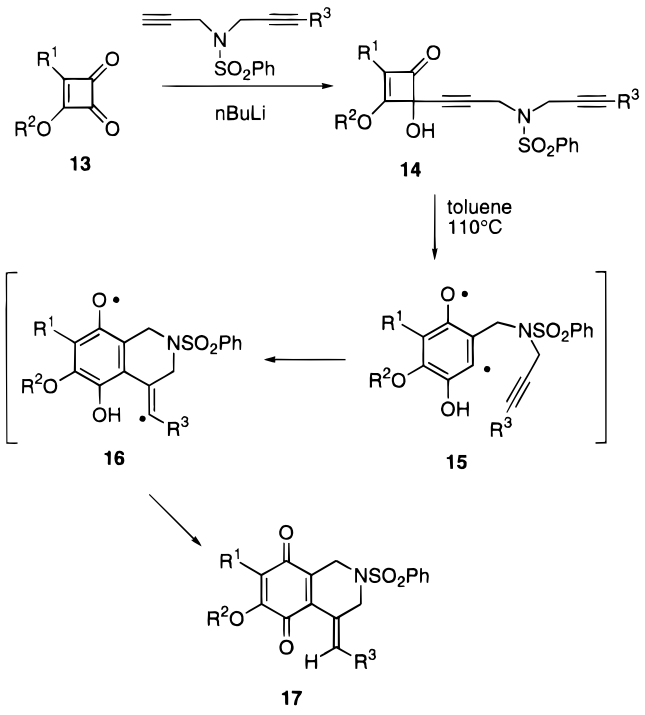
11

12a R = Ph, 90%
12b R = CH_3, 64%

involves treatment of *N*,*N*-dipropynylbenzenesulfonamide **9**[7] with *n*-butyllithium followed by addition of selected electrophiles (trimethylsilyl chloride, acetone, and benzaldehyde) to provide the functionalized diynes **10a**−**c**. In order to eliminate undesired disubstitution pathways, a second method was developed in which the sulfonamide **11**[8] was subjected to Mitsunobu conditions[9] using substituted propargyl alcohols to afford the diynes **12a**,**b** in good to excellent yields.

(8) This compound was obtained in 98% yield from benzenesulfonyl chloride and propargylamine. For an alternate method see: Fr 1,438,772 (C1. C 07*c*), May 13, 1966.

Scheme 3



Entry	R^1	R^2	R^3	Yield 17*
a	Ph	iPr	TMS	44
b	OCH_3	CH_3	TMS	40
c	Bu	iPr	TMS	60
d	OCH_3	CH_3	$(CH_3)_2COH$	50
e	OCH_3	CH_3	Ph	55
f	Bu	iPr	Ph	57

* overall yield from **13**

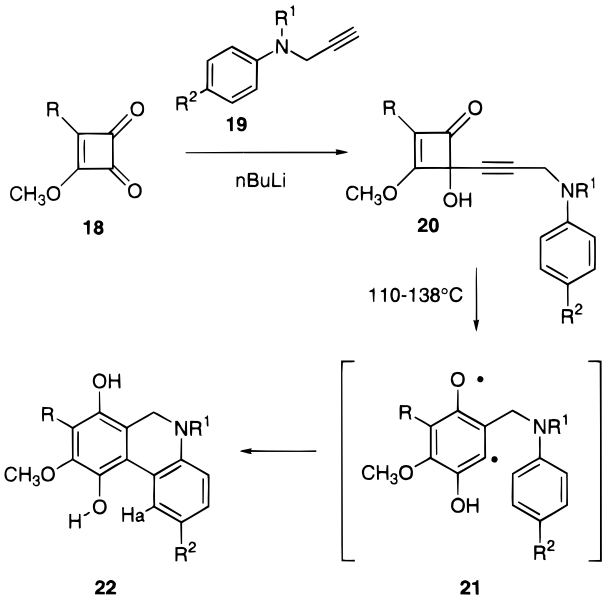
Addition of the lithium salt of the diynes to the cyclobutenediones **13** in THF at −78 °C provided the cyclobutenones **14** (Scheme 3). These were not purified, but thermolyzed directly (toluene, 110 °C) to give the desired piperidinoquinones **17** in 40−60% overall yield. In analogy to the discussion presented above, these transformations are envisaged to occur *via* the intermediate diradicals **15** and **16**.

The structures of the piperidinoquinones **17** were assigned on the basis of their spectral data (^{1}H NMR and ^{13}C NMR) as well as a single crystal X-ray analysis of 3,4-dimethoxy-2,5-dioxo-7-benzylidene-9-*N*-(benzenesulfonyl)bicyclo[4.4.0]deca-1,3-diene (**17e**).[25] The observed *E*-stereochemistry of the exocyclic double bond is in agreement with the proposed configuration of the ultimate diradical intermediate **16**. Since the barrier of inversion for vinyl radicals is low (approximately 2 kcal/mol),[10] this intermediate may actually be in configurational equilibrium, but intramolecular H-atom abstraction provides a direct productive pathway to **17**.

(9) (a) Mitsunobu, O. *Synthesis* **1981**, 1. (b) Comins, D. L.; Gao, J. *Tetrahedron Lett.* **1994**, *35*, 2819.

(10) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*, Part A, 3rd ed.; Plenum Press: New York, 1990; Part A, Chapt. 12, pp 651−719.

Scheme 4



Entry	R	R^1	R^2	Yield 20	Yield 22
a	OCH_3	nBu	H	89	65
b	OCH_3	nBu	OCH_3	-	42*
c	OCH_3	allyl	H	90	63
d	Ph	allyl	H	-	48*
e	OCH_3	tBoc	H	82	70
f	OCH_3	4-pentenyl	H	94	70

* overall yield from **18**

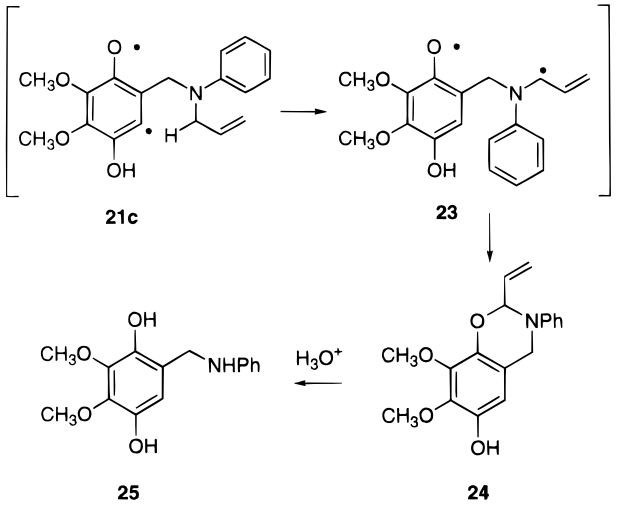
Synthesis of Phenanthridinediols

As an extension of the synthetic scope, cyclobutendiones **18a**,**d** were treated with lithium salts of *N*-arylpropargylamines **19**[11] to give 4-(3-*N*-phenyl-1-propynyl)-4-hydroxycyclobutenones **20a**−**f** in excellent yields (82−94%) (Scheme 4). Thermolyses of these in refluxing toluene or *p*-xylene resulted in the dihydrophenanthridinediols **22a**−**f** (42−70%). In two cases, the crude cyclobutenones **20b** and **20d** were thermolyzed without purification to give dihydrophenanthridinediols **22b** and **22d** in 42% and 48% overall yield from the cyclobutenediones **18b** and **18d**, respectively.

The formation of the dihydrophenanthridinediols **22** is envisaged to involve initial electrocyclic ring opening to the corresponding ketene followed by ring closure to the diradical **21**. The more reactive ring-based radical then undergoes homolytic aromatic substitution to give **22.**[12]

In three cases (**20a**,**c**,**f**), the hydroquinone **25** was also isolated as a minor product (approximately 10% yield). Its formation is also envisaged to arise from the corresponding diradical intermediate. That is, **20c** gives **21c**, which, in addition to the arylation pathway, suffers intramolecular H-atom abstraction from the *N*-allyl group

Scheme 5



to form a new diradical **23.** This leads to aminal **24** upon radical−radical coupling. Standard workup then results in hydrolysis to give hydroquinone **25** (Scheme 5).

The structures of dihydrophenanthridinediols **22a**−**f** were assigned on the basis of their spectral data. Particularly revealing are their ^{1}H NMR spectra which show a characteristic low field aromatic proton (Ha) absorption due to the deshielding effect of the proximal aromatic ring as well as the hydroxy group.[13] As an illustration, this absorption for **22f** appears at δ 8.37 ppm (dd, J = 1.4, 7.7 Hz, 1H). The remaining three aromatic protons absorb at 6.76 ppm (d, J = 8.2 Hz), 6.84 ppm (t, J = 7.5 Hz), and 7.17 ppm (dt, J = 1.4, 8.2 Hz). The two hydroxy groups were observed as singlets at 5.45 ppm and 5.97 ppm. On the basis of these data analogous structure assignments are assumed for the other members of the family.

In spite of the spectral data which are in agreement with the assigned structure, the colors of these compounds are unusual. Most of the hydroquinones **22a**−**f** are deep purple in color. An exception is **22e** which is light yellow. It is assumed that **22a**−**f**, all having a more basic nitrogen than **22e**, exist either as highly colored zwitterions or are in equilibrium with such species, i.e., zwitterions formed by protonation of the amine nitrogen by one of the phenolic hydroxyl groups. Analogies for this are not readily apparent since, to our knowledge, phenanthridine diols such as **22** are not known.

In attempts to obtain supportive chemical evidence for the structure of hydroquinones **22**, selected examples were subjected to oxidizing conditions in anticipation of obtaining the corresponding quinones. Indeed, treatment of **22e** with silver oxide (Ag_2O) provided a nearly quantitative yield of the corresponding quinone **26** (Scheme 6); the hydroquinone **22e** was efficiently regenerated upon treatment of **26** with sodium dithionite.

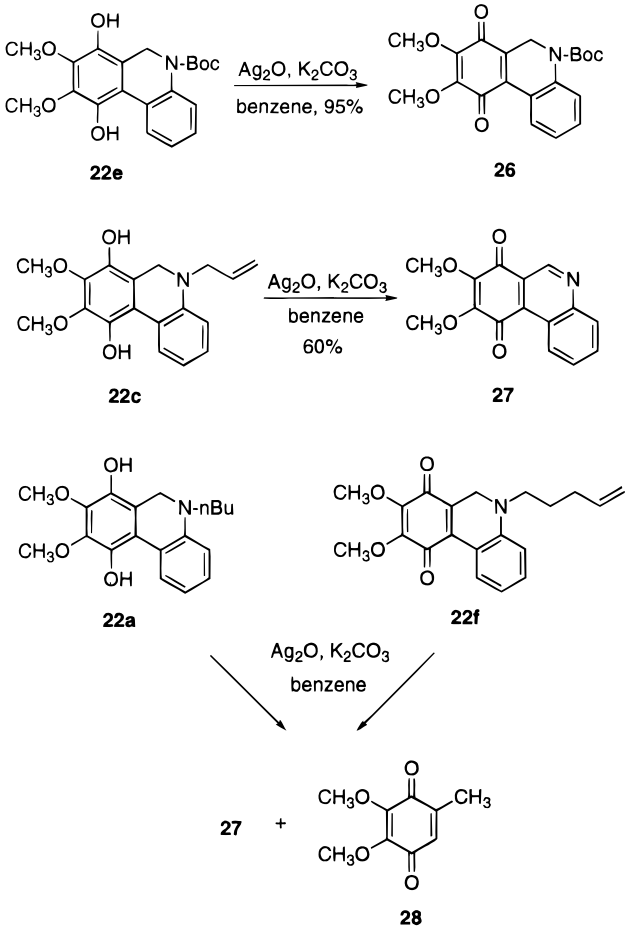
In contrast to the above, unanticipated results were obtained when other members of the **22** series were subjected to the same oxidizing conditions. For example, *N*-allylphenanthridinediol **22c** resulted in oxidative dealkylation to give quinone **27** in 60% isolated yield. Although the dealkylation was unexpected, the overall transformation is consistent with the assigned structure of **22c**. Under similar reaction conditions the *N*-alkyl

(11) (a) Onaka, M.; Umezono, A.; Kawai, M.; Izumi, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 1202. (b) Onaka, M.; Ishikawa, K.; Izumi, Y. *Chem. lett.* **1982**, 1783. (c) Nasimov, E.; Kurbanov, F. K.; Murtazaeva, G. A.; Kuchkarov, A. B. *Uzb. Khim. Zh.* **1982**, *2*, 5. (d) Trost, B. M.; Chen, S. *J. Am. Chem. Soc.* **1986**, *108*, 6053.

(12) For a review on homolytic aromatic substitutions, see: Waters, W. A. *Free Radical Reactions*; Butterworth: London, 1987; Chapter 3, pp 25−45.

(13) Krane, B. D.; Fagbule, M. O.; Shamma, M. *J. Nat. Prod.* **1984**, *47*, 1.

Scheme 6



examples, **22a** and **22f**, gave complex reaction mixtures from which **27** (5−14%) and 2,3-dimethoxy-5-methyl-1,4-benzoquinone (**28**) (10−16%) were the only isolable products. The formation of **28** is particularly intriguing and remains a mechanistic puzzle.

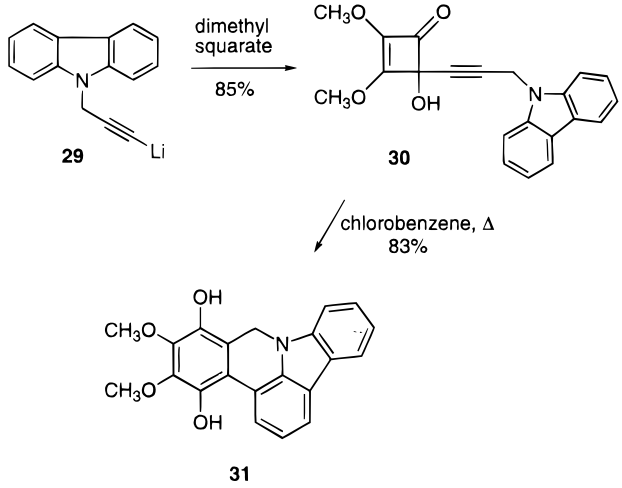
The scope of the phenanthridine synthesis was expanded to include the preparation of selected examples having highly condensed ring systems, e.g., indolophenanthridines, isoindoloindoles, and benzophenanthridines. Thus, treatment of dimethyl squarate with the *N*-propargylcarbazole lithium reagent **29**[14] provided cyclobutenone **30** in 85% yield (Scheme 7). Thermolysis of this in refluxing chlorobenzene for 1.75 h gave the pentacyclic indolophenanthridine **31** as a light blue crystalline solid in good yield (83%).

The ^{1}H NMR spectrum of **31** provides characteristic structure information; the characteristic low field aromatic absorption appears at d, 8.50 ppm (dd, J = 0.7, 7.7 Hz); the two hydroxy groups absorb as singlets at 5.54 and 6.15 ppm, and the absorption for the other six aromatic protons appear at 7.19−8.10 ppm.

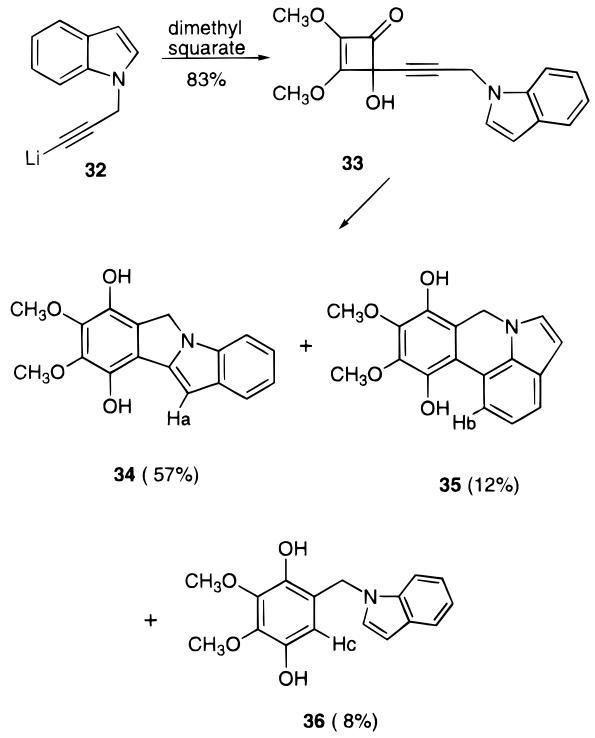
Synthesis of an isoindoloindole as well as a pyrrolophenanthridinediol stems from treatment of dimethyl squarate with the lithium salt of *N*-propargylindole (**32**)[14] to provided cyclobutenone **33** in 83% yield. Subsequent thermolysis (2 h, refluxing chlorobenzene) of this gave the tetracyclic isoindoloindole **34** (57%) and pyrrolophenanthridinediol **35** (12%) along with a nonannulated hydroquinone **36** (8%) (Scheme 8).

(14) The synthesis of this compound differs slightly from that reported by Broggini, G.; Bruche, L.; Zecchi, G. *J. Chem. Soc., Perkin. Trans. 1* **1990**, 533.

Scheme 7



Scheme 8

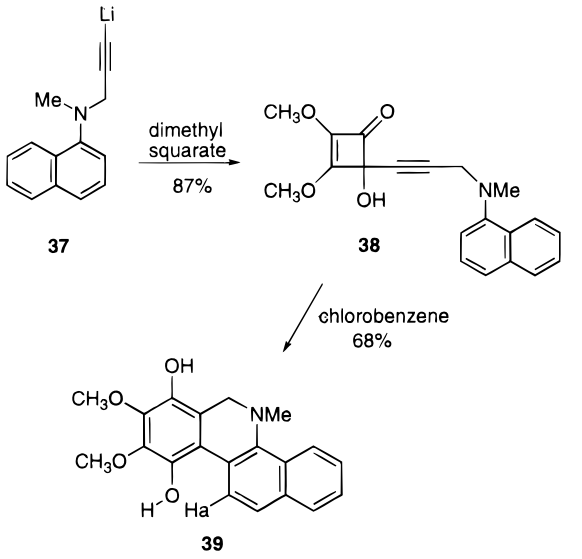


Pyrrolophenanthridinediol **35** is envisaged to arise in a manner similar to that of the other phenanthridinediols, i.e. intramolecular homolytic aromatic substitution at the intermediate diradical stage. Isoindoloindole **34** is formed analogously except radical attack takes place on the pyrrole ring. The hydroquinone **36** presumably arises from H-atom abstractions from unspecified sources by the diradical intermediate.

The ^{1}H NMR spectral data for **34**−**36** are consistent with their assigned structures. Both **34** and **35** show absorption for five aromatic protons. The proton Ha in **34** appears at 6.63 ppm as a singlet, while the low field absorption for proton Hb in **35** appears at 8.20 ppm as a doublet (J = 7.7 Hz). The spectrum of compound **36** shows absorption for seven aromatic protons with the characteristic proton Hc showing its absorption at 6.27 ppm as a singlet.

A new synthetic route to benzophenanthridine (Scheme 9) is particularly noteworthy since this ring system is the framework for a large class of alkaloids.[13,15] Addition of

Scheme 9

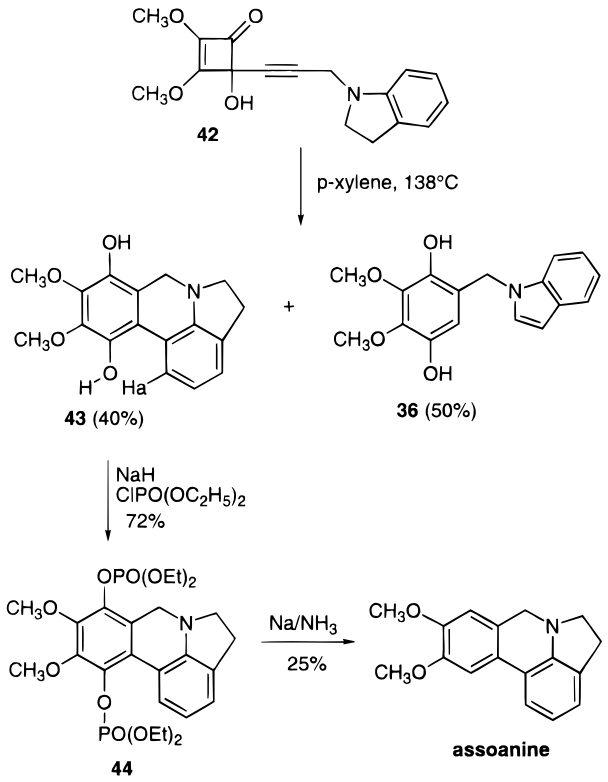


the lithium salt of *N*-methyl-*N*-propargyl-1-naphthylamine (**37**)[16] to dimethyl squarate in THF at −78 °C provided cyclobutenone **38** in 87% yield, thermolysis (chlorobenzene, 2 h) of which gave benzophenanthridine **39** in 68% yield. The characteristic low field aromatic absorption for Ha appears at 8.55 ppm (d, $J = 8.7$ Hz), and the two hydroxy groups appear as singlets at 5.46 ppm and 6.04 ppm.

Synthesis of Assoanine

Finally, the 4-alkynyl-4-hydroxycyclobutenone ring expansion reaction was applied in a total synthesis of assoanine (**40**), a member of a series of biologically active pyrrolophenanthridine alkaloids isolated from various *Crinum* species (*Amaryllidaceae*).[17−21] The synthesis (Scheme 10) begins by treating indoline with sodium hydride and propargyl bromide in DMF to provide *N*-propargyl indoline in 93% yield.[22] Addition of the lithium salt of this compound to dimethyl squarate in THF at −78 °C gave cyclobutenone **42** in 87% yield. This adduct was subjected to thermolysis in refluxing *p*-xylene

Scheme 10



for 2 h to afford the desired pyrrolophenanthridine **43** (40%) along with a nonannulated hydroquinone **36** (50%). Formation of the former is in analogy to the above described arylation reactions. The latter apparently arises via an intramolecular H-atom abstraction from the indoline moiety at the diradical stage, thus providing the nonannulated hydroquinone bearing the indole group. This product was shown to be identical to the minor product previously noted as arising in the thermolysis of **33**.

The ^{1}H NMR spectrum of **43** shows the previously noted characteristic aromatic proton Ha at 8.06 ppm (d, $J = 7.7$ Hz). The two hydroxy groups appear as singlets at 5.56 and 5.97 ppm, and the two pyrrolidinyl methylene groups appear as triplets at 3.00 ppm and 3.31 ppm while the benzylic protons appear at 4.10 ppm as a singlet.

A variety of conditions were employed to remove the phenolic hydroxy groups from **43** and thus obtain the natural product.[23] The best method, although still inefficient, involved reductive cleavage of diethyl phosphate ester **44.** This derivative was formed in 72% yield upon treatment of **43** with sodium hydride in THF followed by addition of diethyl chlorophosphonate. Reductive removal of the phosphate ester groups using sodium in liquid ammonia provided the natural product assoanine (**40**) in 25% yield. The structure of assoanine is based on comparison of its spectral data to those reported in the literature.[17,18] Particularly revealing is the comparison of the ^{13}C NMR spectra where all 16 chemical shifts in the observed carbon-13 spectrum matched to within

(15) (a) For a review prior to 1984 on this subject, see: Simanek, V. *The Alkaloids*; Brossi, A., Ed.; Academic Press: Orlando, 1985; Vol. 26, p 185. (b) Ishii, H.; Ichikawa, Y.; Kawanabe, E.; Ishikawa, M.; Ishikawa, T.; Kuretani, K.; Inomata, M.; Hoshi, A. *Chem. Pharm. Bull.* **1985**, *33*, 4139. (c) Carty, A.; Elliott, W.; Lenior, G. M. *Can. J. Chem.*, **1984**, 2435. (d) Kessar, S. V.; Gupta, Y. P.; Dhingra, K.; Sharma, G. S.; Narula, S. *Tetrahedron Lett.* **1977**, *17*, 1459. (e) Ishii, H.; Ishikawa, T.; Watanabe, T.; Ichikawa, Y.; Kawanabe, E. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2283. (f) Hanaoka, M.; Kobayashi, N.; Shimada, K.; Mukai, C. *J. Chem. Soc., Perkin Trans. 1* **1987**, 677. (g) Olugbade, T. A.; Waigh, R. D.; Mackay, S. P. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2657. (h) Sotomayor, N.; Dominguez, E.; Lete, E. *Tetrahedron, Lett.* **1994**, *35*, 2973. (i) Seraphin, D.; Lynch, M.; Duval. O. *Tetrahedron Lett.* **1995**, *36*, 5731.

(16) (a) Katritzky, A. R.; Balck, M.; Fan, W. *J. Org. Chem.* **1991**, *56*, 5045. (b) Scheurer, H.; Zsindely, J.; Schmid, H. *Helv. Chim. Acta* **1973**, *56*, 478.

(17) Liabres, J. M.; Viladomat, F.; Bastida, J.; Codina, C.; Rubiralta, M. *Phytochemistry* **1986**, *25*, 2637.

(18) Parnes, J. S.; Carter, D. S.; Kurz, L. J.; Flippin, L. A. *J. Org. Chem.* **1994**, *59*, 3497.

(19) (a) Ghosal, S.; Rao, P. H.; Jaiswal, D. K.; Kumar, Y.; Frahm, A. W. *Phytochemistry* **1981**, *20*, 2003. (b) Ghosal, S.; Saini, K. S.; Frahm, A. W. *Ibid.* **1983**, *22*, 2305.

(20) Grundon, M. F. *Nat. Prod. Rep.* **1989**, *6*, 79.

(21) (a) Chattopadhyay, S. C.; Chattopadhyay, U.; Mathur, P. P.; Saini, K. S.; Ghosal, S. *Planta Med.* **1983**,*49*, 252. (b) Cheng, R. K. Y.; Yan, S. J.; Chen, C. C. *J. Med. Chem.* **1978**, *21*, 199.

(22) Torregrosa, J.; Baboulene, M.; Speziale, V.; Lattes, A. *J. Organomet. Chem.* **1983**, *244*, 311.

(23) For deoxygenation of phenols, see: (a) Rossi, R. A.; Bunnett, J. F. *J. Org. Chem.* **1973**, *38*, 2314. (b) Sebok, P.; Timar, T.; Eszenyi, T. *J. Org. Chem.* **1994**, *59*, 6318. (c) Subramanian, L. R. *Synthesis* **1984**, 481. (d) Hussey, B. J.; Johnstone, R. A. W. *Tetrahedron* **1982**, *38*, 3775. (e) Cabri, W.; Bernardinis, S. D.; Francalanci, F.; Penco, S.; Santi, R. *J. Org. Chem.* **1990**, *55*, 350. (f) Clauss, K.; Jensen, H. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 918. (g) Welch, S. C.; Walters, M. E. *J. Org. Chem.* **1978**, *43*, 4797.

0.3 ppm (average deviation ± 0.1 ppm) the published spectrum obtained for the natural product.

Conclusions

In conclusion, the following significant points arising from the study outlined here are noted: (1) ring expansions of 4-hydroxy-4-[4-*N*-(benzenesulfonyl)-4-aza-1,6-alkadiynyl]cyclobutenones provide a general route to piperidinoquinones; (2) dihydrophenanthridinediols are formed from the thermolysis of 4-hydroxy-4-(3-*N*-phenyl-1-propynylamino)cyclobutenones, and these hydroquinones are members of a previously unknown class of compounds; (3) a benzophenanthridine was synthesized from 4-(3-*N*-naphthalenyl-1-propynylamino)cyclobutenone in only four steps and thus provided a potentially general route to the ring system found in a large family of alkaloids; (4) assoanine was synthesized from dimethyl squarate and indoline in five steps. Although the overall yield is low (5%), the route is direct and provides methodology that is potentially useful for the construction of a variety of related alkaloids and analogs.

Experimental Section

General Procedure. All air or water sensitive reactions were run in flame dried glassware under an atmosphere of dry (Drierite) nitrogen. Tetrahydrofuran was freshly distilled from calcium hydride then sodium/benzophenone. Other anhydrous solvents (benzene, toluene, and *p*-xylene) were freshly distilled from calcium hydride. Commercial reagents were used without any further purification unless otherwise noted.

***N*-(2-Propynyl)-*N*-[3-(trimethylsilyl)-2-propynyl]benzenesulfonamide (10a).** A solution of nBuLi (0.687 mL, 1.6 M in hexanes, 1.1 mmol) in THF (10 mL) was cooled to −78 °C. This was then added *via cannula* to a solution of *N*,*N*-bis(2-propynyl)benzenesulfonamide (**9**) (233 mg, 1.0 mmol) in THF (10 mL) at −78 °C. The resulting alkynyllithium solution was stirred at −78 °C for 30 min, and chlorotrimethylsilane (163 mg, 1.5 mmol) was added. The resulting solution was stirred at −78 °C for 1 h. The mixture was then quenched with ammonium chloride (10%, 20 mL), and the aqueous layer was extracted with EtOAc (2 × 15 mL). The combined organic portion was dried over magnesium sulfate and concentrated *in vacuo*. Chromatography (hexanes/EtOAc = 8:1) gave product **10a** (152 mg, 50%) as a light yellow solid: mp 66−67 °C; IR ($CDCl_3$) 2256, 1479, 1165 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.047 (s, 9H), 2.13 (t, J = 2.5 Hz, 1H), 4.14 (d, J = 2.5 Hz, 2H), 4.20 (s, 2H), 7.48−7.52 (m, 2H), 7.57−7.59 (m, 1H), 7.83−7.85 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 132.9, 128.8, 127.6, 97.1, 91.2, 76.1, 73.8, 37.1, 36.1, −0.485; exact mass calcd for $C_{15}H_{20}NO_2SiS$ $(MH)^+$: 306.0984, found 306.0987.

***N*-(2-Propynyl)-*N*-(4-methyl-4-hydroxy-2-pentynyl)benzenesulfonamide (10b).** Using acetone as the trap and in analogy to the above procedure for **10a**, compound **10b** (1.33 g, 62%) was obtained as a light yellow oil from **9** (1.72 g, 7.38 mmol): IR (neat) 3509, 3288, 2122 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 6H), 1.96 (s, 1H), 2.14 (t, J = 2.4 Hz, 1H), 4.12 (d, J = 2.4 Hz, 2H), 4.19 (s, 2H), 7.48−7.51 (m, 2H), 7.53−7.59 (m, 1H), 7.81−7.84 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 133.0, 128.9, 127.8, 90.6, 76.2, 74.1, 73.9, 64.7, 36.5, 36.3, 31.0; exact mass calcd for $C_{15}H_{18}NO_3S$ $(MH)^+$: 292.1007, found 292.1013.

***N*-(2-Propynyl)-*N*-(4-phenyl-4-hydroxy-2-butynyl)benzenesulfonamide (10c).** Using benzaldehyde as the trap and in analogy to the above **10c** (1.22 g, 49%) was obtained as a light-yellow oil from **9** (1.72 g, 7.38 mmol): IR (neat) 3498, 3288, 2360, 2122 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.14 (t, J = 2.5 Hz, 1H), 2.18 (s, 1H), 4.14 (d, J = 2.5 Hz, 2H), 4.27 (d, J = 1.8 Hz, 2H), 5.26 (d, J = 1.5 Hz, 1H), 7.31−7.37 (m, 5H), 7.42−7.46 (m, 2H), 7.52−7.55 (m, 1H), 7.81−7.83 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.9, 138.1, 133.0, 128.9, 128.5, 128.4, 127.7, 126.4, 85.6, 78.8, 76.1, 74.2, 64.2, 36.6, 36.5; exact mass calcd for $C_{19}H_{18}NO_3S$ $(MH)^+$: 340.1007, found 340.1023.

***N*-(2-Propynyl)-*N*-(3-phenyl-2-propynyl)benzenesulfonamide (12a).** To a solution of **11**[8] (1.40 g, 7.18 mmol), triphenylphosphine (1.88 g, 7.18 mmol), and 3-phenyl-2-propyn-1-ol (1.42 g, 10.77 mmol) in THF (70 mL) was added a solution of diethyl azodicarboxylate (1.25 g, 7.18 mmol) in THF (10 mL) at 0 °C in 15 min. The mixture was stirred at room temperature overnight and then concentrated *in vacuo*. Chromatography (hexanes/EtOAc = 3:1) gave product **12a** (2 g, 90%) as a yellow oil: IR (neat) 3425, 3291, 2245 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.16 (t, J = 2.2 Hz, 1H), 4.22 (d, J = 2.2 Hz, 2H), 4.43 (s, 2H), 7.19−7.21 (m, 2H), 7.23−7.30 (m, 3H), 7.47−7.51 (m, 2H), 7.54−7.57 (m, 1H), 7.87−7.89 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 138.3, 133.0, 131.6, 128.9, 128.6, 128.2, 127.8, 122.0, 85.9, 81.2, 76.3, 74.0, 37.2, 36.4; exact mass calcd for $C_{18}H_{15}NO_2S$: 309.0823, found 309.0813.

***N*-(2-Propynyl)-*N*-(2-butynyl)benzenesulfonamide (12b).** In analogy to the above procedure for **12a**, compound **12b** (800 mg, 64%) was obtained as a light yellow solid from **11** (1.40 g, 7.18 mmol): mp 57−58 °C; IR ($CDCl_3$) 3307, 3070, 1447, 1095 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.61 (t, J = 2.3 Hz, 3H), 2.12 (t, J = 2.3 Hz, 1H), 4.10 (d, J = 2.3 Hz, 2H), 4.12 (d, J = 2.4 Hz, 2H), 7.46−7.57 (m, 2H), 7.80−7.83 (m, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 138.1, 132.8, 128.7, 127.7, 82.1, 76.7, 76.3, 73.7, 36.6, 36.1, 3.3; exact mass calcd for $C_{13}H_{12}NO_2S$ $(M - H)^+$: 246.0589, found 246.0599.

General Procedure for the Synthesis of Cyclobutenones 14a−f. 2-Phenyl-3-isopropoxy-4-[4-*N*-(benzenesulfonyl)-4-aza-7-(trimethylsilyl)-1,6-heptdiynyl]-4-hydroxy-2-cyclobuten-1-one (14a). To a solution of **10a** (122 mg, 0.4 mmol) in THF (5 mL) at −78 °C was added nBuLi (0.25 mL, 1.6 M in hexanes, 0.4 mmol), and the solution was stirred for 30 min at the same temperature and was transferred to a solution of 2-phenyl-3-isopropoxycyclobutenedione (87 mg, 0.4 mmol) in THF (5 mL) *via cannula*. The resulting solution was stirred for 40 min at −78 °C, quenched with saturated ammonium chloride (10 mL), and extracted with diethyl ether (2 × 10 mL). The combined organic portion was washed with brine (15 mL), dried over magnesium sulfate, and concentrated *in vacuo*. The crude product (predominantly one spot by thin layer chromatography) was subjected to thermolysis without further purification.

3-Phenyl-4-isopropoxy-2,5-dioxo-7-[(*E*)-2-(trimethylsilyl)ethylidene]-9-*N*-(benzenesulfonyl)bicyclo[4.4.0]deca-1,3-diene (17a). The crude cyclobutenone **14a** in toluene (25 mL) was added dropwise (40 min) under nitrogen to refluxing toluene (150 mL), and the resulting solution was refluxed for an additional 20 min. The solution was cooled to room temperature and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 4:1) gave **17a** [91 mg, 44% overall yield from **13a** (87 mg, 0.4 mmol)] as a brown oil: IR ($CDCl_3$) 1668, 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.30 (s, 9H), 1.08 (d, J = 6.2Hz, 6H), 3.96 (s, 2H), 4.16 (s, 2H), 4.43 (heptet, J = 6.2 Hz, 1H), 7.08 (s, 1H), 7.25−7.27 (m, 2H), 7.37−7.40 (m, 3H), 7.50−7.53 (m, 2H), 7.57−7.59 (m, 1H), 7.79−7.81 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 185.8, 183.0, 154.7, 143.2, 137.3, 136.3, 135.5, 133.6, 133.4, 130.5, 130.2, 129.9, 129.4, 128.8, 128.0, 127.9, 76.7, 49.0, 44.0, 22.7, 0.071; exact mass calcd for $C_{28}H_{32}O_5SiS$ $(MH)^+$: 522.1770, found 522.1766.

3,4-Dimethoxy-2,5-dioxo-7-[(*E*)-2-(trimethylsilyl)ethylidene]-9-*N*-(benzenesulfonyl)bicyclo[4.4.0]deca-1,3-diene (17b). In analogy to the above procedure, compound **17b** [71 mg, 40% overall yield from **13b** (57 mg, 0.4 mmol)] was obtained as a red-orange oil: IR ($CDCl_3$) 1659 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.26 (s, 9H), 3.88 (s, 2H), 3.96 (s, 3H), 3.97 (s, 3H), 4.08 (s, 2H), 7.08 (s, 1H), 7.53−7.60 (m, 3H), 7.77−7.80 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 182.6, 182.4, 144.9, 144.1, 143.7, 136.8, 135.9, 133.5, 133.2, 132.5, 129.2, 127.6, 61.2, 61.1, 48.7, 43.3, −0.304; exact mass calcd for $C_{21}H_{25}NO_6SiS$: 447.1172, found 447.1179.

3-Butyl-4-isopropoxy-2,5-dioxo-7-[(*E*)-2-(trimethylsilyl)ethylidene]-9-*N*-(benzenesulfonyl)bicyclo[4.4.0]deca-1,3-diene (17c). In analogy to the above procedure, compound **17c** [120 mg, 60% overall yield from **13c** (78.4 mg, 0.4 mmol)]

was obtained as a red oil: IR ($CDCl_3$) 1669, 1636 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.26(s, 9H), 0.89 (t, J = 7.0 Hz, 3H), 1.26−1.36 (m, 10H), 2.37 (t, J = 7.3 Hz, 2H), 3.89 (s, 2H), 4.09 (s, 2H), 4.73 (heptet, J = 6.2 Hz, 1H), 6.96 (s, 1H), 7.48−7.58 (m, 3H), 7.76−7.79 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 186.3, 182.3, 155.3, 142.4, 137.3, 135.9, 135.2, 133.1, 132.9, 129.2, 127.7, 75.6, 48.8, 43.7, 30.7, 22.9, 22.8, 22.7, 13.8, −0.16; exact mass calcd for $C_{26}H_{35}NO_5SiS$: 501.2005, found 501.2010.

3,4-Dimethoxy-2,5-dioxo-7-[(*E*)-3-methyl-3-hydroxy-1-butylidene]-9-*N*-(benzenesulfonyl)bicyclo[4.4.0]deca-1,3-diene (17d). In analogy to the above procedure, compound **17d** [150 mg, 50% overall yield from **13b** (100 mg, 0.7 mmol)] was obtained as an orange-red solid: mp 139−140 °C; IR ($CDCl_3$) 1669, 1636 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.47 (s, 6H), 1.95 (s, 1H), 3.95 (s, 3H), 3.97 (s, 3H), 4.09 (s, 2H), 4.33 (s, 2H), 6.86 (s, 1H), 7.50−7.53 (m, 2H), 7.56−7.58 (m, 1H), 7.82−7.83 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 182.4, 146.4, 146.3, 145.0, 143.8, 136.6, 134.4, 133.9, 133.0, 129.2, 127.6, 123.6, 72.3, 61.3, 61.2, 43.8, 43.2, 31.1, 31.0; exact mass calcd for $C_{21}H_{23}NO_7S$ $(MH)^+$: 434.1273, found 434.1237.

3,4-Dimethoxy-2,5-dioxo-7-(*E*)-benzylidene-9-*N*-(benzenesulfonyl)bicyclo[4.4.0]deca-1,3-diene (17e). In analogy to the above procedure, compound **17e** [123 mg, 55% overall yield from **13b** (71 mg, 0.5 mmol)] was obtained as an orange-red solid: mp 155−156 °C; IR ($CDCl_3$) 1649, 1593 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.97 (s, 3H), 4.00 (s, 3H), 4.20 (s, 2H), 4.24 (s, 2H), 7.25−7.27 (m, 2H), 7.36−7.38 (m, 1H), 7.42−7.47 (m, 4H), 7.54−7.56 (m, 1H), 7.65−7.67 (m, 2H), 7.82 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 182.4, 182.2, 145.0, 143.9, 139.5, 136.7, 135.8, 133.8, 133.6, 133.0, 129.3, 129.1, 128.7, 128.6, 127.5, 123.8, 61.3, 61.2, 45.0, 43.3; exact mass calcd for $C_{24}H_{21}NO_6S$: 451.1089, found 451.1098.

3-Butyl-4-isopropoxy-2,5-dioxo-7-benzylidene-9-*N*-(benzenesulfonyl)bicyclo[4.4.0]deca-1,3-diene (17f). In analogy to the above procedure, compound **17f** [200 mg, 57% overall yield from **13c** (137 mg, 0.7 mmol)] was obtained as a red oil: IR ($CDCl_3$) 1665, 1635 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.92 (t, J = 7.3 Hz, 3H), 1.28 (d, J = 6.2 Hz, 6H), 1.31−1.41 (m, 4H), 2.40 (t, J = 7.3 Hz, 2H), 4.20 (d, J = 1.1 Hz, 2H), 4.25 (s, 2H), 4.73 (heptet, J = 6.2 Hz, 1H), 7.25−7.28 (m, 2H), 7.34−7.38 (m, 1H), 7.42−7.47 (m, 4H), 7.52−7.56 (m, 1H), 7.65−7.67 (m, 2H), 7.73 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 185.8, 182.3, 155.3, 138.3, 136.7, 135.8, 135.2, 134.1, 133.2, 133.0, 129.3, 129.1, 128.6, 128.4, 127.6, 124.1, 75.7, 45.0, 43.6, 30.7, 22.9, 22.8, 13.8; exact mass calcd for $C_{29}H_{31}NO_5S$: 505.1923, found 505.1944.

***N*-n-Butyl-*N*-propargyl-*p*-anisidine (19b).** A mixture of *N*-n-butyl-*p*-anisidine (1.03 g, 5.75 mmol), propargyl bromide (1.71 g, 80% in toluene, 11.5 mmol), and potassium carbonate (952 mg, 6.9 mmol) in acetone (120 mL) was refluxed for 21 h. The mixture was diluted with diethyl ether (50 mL), washed with water (30 mL), and extracted with diethyl ether (3 × 40 mL). The combined organic portion was washed with water (40 mL) and brine (50 mL), dried, and concentrated *in vacuo*. Chromatography (hexanes/EtOAc = 8:1) gave product **19b** (1.13 g, 91%) as a yellow oil: IR (neat) 2054 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, J = 7.3 Hz, 3H), 1.38 (hextet, J = 7.6 Hz, 2H), 1.53−1.59 (m, 2H), 2.17 (t, J = 2.3 Hz, 1H), 3.23 (t, J = 7.4 Hz, 2H), 3.75 (s, 3H), 3.93 (d, J = 2.4 Hz ,2H), 6.85 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.6, 142.8, 116.8, 114.3, 80.0, 71.8, 55.3, 51.5, 41.1, 29.4, 20.2, 13.8; exact mass calcd for $C_{14}H_{19}NO$: 217.1467, found 217.1472.

***N*-(*tert*-Butoxycarbonyl)-*N*-propargylaniline (19e).** To a solution of aniline (1.86 g, 20 mmol) and triethylamine (3.03 g, 30 mmol) in chloroform (40 mmol) was added di-*tert*-butyl dicarboxylate (6.55 g, 30 mmol) at 0 °C. The mixture was stirred at room temperature for a few hours and then washed with 3 N NaOH. The aqueous layer was extracted with methylene chloride (3 × 40 mL). The combined organic layer was washed with brine, dried, and concentrated *in vacuo*. The crude product was dissolved in THF−DMSO (120 mL, 1:1), and sodium hydride (1.44 g, 50% oil suspension, 30 mmol) was added. The resulting solution was stirred at room temperature for 3 h and propargyl bromide (4.46 g, 80% in toluene, 30 mmol) was added at 0 °C. The mixture was stirred at room temperature overnight, quenched with saturated ammonium chloride (70 mL), and extracted with diethyl ether (2 × 40 mL). The organic layer was washed with brine, dried, and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 8:1) gave **19e** (3.97 g, 86%) as a yellow oil: IR (neat) 2360, 2120 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.49 (s, 9H), 2.28 (t, J = 2.4 Hz, 1H), 4.40 (d, J = 3.4 Hz, 2H), 7.24−7.30 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.7, 141.9, 128.5, 126.0, 80.7, 79.8, 71.7, 39.5, 28.1; exact mass calcd for $C_{14}H_{17}NO_2$: 231.1259, found 231.1257.

***N*-(4-Pentenyl)-*N*-propargylaniline (19f).** In analogy to the above procedure, **19f** (1.96 g, 90%) was obtained as a yellow oil starting with *N*-(4-pentenyl)aniline (1.77 g, 11 mmol): IR (neat) 2934 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.80 (quintet, J = 7.3 Hz, 2H), 2.16−2.21 (m, 2H), 2.23 (t, J = 2.2 Hz, 1H), 3.41 (t, J = 7.3 Hz, 2H), 4.06 (bs, 2H), 5.06−5.14 (m, 2H), 5.88−5.94 (m, 1H), 6.82−6.84 (m, 1H), 6.88 (d, J = 7.7 Hz, 2H), 7.29−7.33 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 137.9, 129.0, 117.5, 115.0, 113.6, 80.1, 71.6, 50.7, 40.1, 31.1, 26.4; exact mass calcd for $C_{14}H_{17}N$: 199.1361, found 199.1361.

2,3-Dimethoxy-4-hydroxy-4-[3-(*N*-*n*-butyl-*N*-phenylamino)-1-propynyl]-2-cyclobuten-1-one (20a). To a solution of **19a** (449 mg, 2.4 mmol) in THF (20 mL) at −78 °C was added nBuLi (1.5 mL, 1.6 M in hexanes, 2.4 mmol), and the solution was stirred for 15 min and then transferred to a solution of dimethyl squarate (284 mg, 2.0 mmol) in THF (20 mL) *via cannula*. The resulting solution was stirred for 30 min at −78 °C, quenched with saturated ammonium chloride (40 mL), and extracted with diethyl ether (2 × 25 mL). The combined organic portion was washed with brine (30 mL), dried over magnesium sulfate, and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 4:1) gave **20a** (584 mg, 89%) as a brown viscous oil: IR (neat) 3373, 2359, 2249, 1780, 1633 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J = 7.3 Hz, 3H), 1.35 (hextet, J = 7.5 Hz, 2H), 1.58 (quintet, J = 7.6 Hz, 2H), 3.30 (t, J = 7.5 Hz, 2H), 3.89 (s, 3H), 4.03 (s, 3H), 4.06 (d, J = 3.0 Hz, 2H), 4.28 (s, 1H), 6.72−6.75 (m, 1H), 6.78−6.80 (m, 2H), 7.20−7.23 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.9, 164.9, 147.9, 135.1, 128.9, 117.5, 113.7, 85.9, 78.2, 77.9, 59.7, 58.3, 51.0, 40.5, 29.3, 20.3, 13.8; exact mass calcd for $C_{19}H_{23}NO_4$: 329.1627, found 329.1612.

2,3-Dimethoxy-4-hydroxy-4-[3-[*N*-*n*-butyl-*N*-(4-methoxyphenyl)amino]-1-propynyl]-2-cyclobuten-1-one (20b). In analogy to the above, **19b** (238 mg, 1.1 mmol) was converted to the cyclobutenone **20b**. The crude product (approximately 70% pure by ^1H NMR analysis) was subjected to thermolysis without further purification.

2,3-Dimethoxy-4-hydroxy-4-[3-(*N*-allyl-*N*-phenylamino)-1-propynyl]-2-cyclobuten-1-one (20c). In analogy to the above procedure, **20c** (564 mg, 90%) was obtained as a yellow solid starting with **18c** (284 mg, 2.0 mmol): mp 75−78 °C; IR ($CDCl_3$) 3577, 3359, 2245, 1781, 1626 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 1H), 3.93 (m, 5H), 4.07 (s, 3H), 4.08 (bs, 2H), 5.15−5.28 (m, 2H), 5.86 (dddd, J = 5.1, 10.2, 15.3, 17.0 Hz, 1H), 6.75−6.84 (m, 3H), 7.20−7.26 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.7, 164.7, 148.2, 135.4, 133.8, 129.0, 118.1, 116.8, 114.2, 85.8, 78.3, 78.0, 59.9, 58.5, 53.7, 40.1; exact mass calcd for $C_{18}H_{19}NO_4$: 313.1314, found 313.1314.

2-Phenyl-3-methoxy-4-hydroxy-4-[3-(*N*-allyl-*N*-phenylamino)-1-propynyl]-2-cyclobuten-1-one (20d). In analogy to the above, **19c** (157 mg, 0.92 mmol) was converted to **20d**. The crude product (predominantly one spot by thin layer chromatography) was subjected to thermolysis without further purification.

2,3-Dimethoxy-4-hydroxy-4-[3-[*N*-(*tert*-butoxycarbonyl)-*N*-phenylamino]-1-propynyl]-2-cyclobuten-1-one (20e). In analogy to the above procedure, **20e** (610 mg, 82%) was obtained as a viscous dark red oil starting with **18e** (284 mg, 2.0 mmol): IR (neat) 3378, 1781, 1697, 1645 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 9H), 3.33 (s, 1H), 3.95 (s, 3H), 4.10 (s, 3H), 4.44 (s, 2H), 7.26−7.34 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.5, 164.8, 153.9, 141.6, 135.1, 128.5, 126.3, 126.2, 85.2, 81.1, 78.3, 59.7, 58.4, 39.9, 28.0; exact mass calcd for $C_{20}H_{23}NO_6$: 373.1525, found 373.1525.

2,3-Dimethoxy-4-hydroxy-4-[3-[*N*-(4-pentenyl)-*N*-phenylamino]-1-propynyl]-2-cyclobuten-1-one (20f). In analogy to the above procedure, **20f** (963 mg, 94%) was

obtained as a yellow oil starting with **18f** (426 mg, 3.0 mmol): IR ($CDCl_3$) 3378, 1779, 1651, 1633 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.74 (quintet, J = 7.3 Hz, 2H), 2.11 (q, J = 7.1 Hz, 2H), 3.34 (t, J = 7.3 Hz, 2H), 3.65−3.68 (m, 1H), 3.93 (s, 3H), 4.06 (s, 3H), 4.09 (s, 2H), 5.02−5.08 (m, 2H), 5.77−5.91 (m, 1H), 6.74−6.82 (m, 3H), 7.24−7.26 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.7, 164.8, 147.9, 137.9, 135.2, 129.0, 117.6, 114.9, 113.8, 85.9, 78.2, 78.0, 59.8, 58.4, 50.7, 40.6, 31.0, 26.2; exact mass calcd for $C_{20}H_{23}NO_4$: 341.1627, found 341.1617.

5-Butyl-5,6-dihydro-8,9-dimethoxy-7,10-phenanthridinediol (22a). A solution of **20a** (395 mg, 1.20 mmol) in toluene (120 mL) was added dropwise to a refluxing toluene (250 mL, under N_2) during a 1 h 40 min period. The solution was refluxed for an additional 20 min and cooled to room temperature, and the solvent was removed *in vacuo*. Chromatography (hexanes/ethyl acetate = 3:1) gave product **22a** (255 mg, 65%) as a purple oil: IR ($CDCl_3$) 3520,1633, 1599 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.97 (t, J = 7.3 Hz, 3H), 1.41 (hextet, J = 7.7 Hz, 2H), 1.69 (quintet, J = 7.3 Hz, 2H), 3.28 (t, J = 7.7 Hz, 2H), 3.92 (s, 3H), 3.94 (s, 3H), 4.19 (s, 2H), 5.40 (s, br, 1H), 5.93 (s, br, 1H), 6.76 (d, J = 8.01 Hz, 1H), 6.82 (dt, J = 1.1, 7.7 Hz, 1H), 7.17 (dt, J = 1.5, 8.0 Hz, 1H), 8.37 (dd, J = 1.4, 7.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.2, 139.6, 138.3, 137.9, 136.8, 128.5, 127.9, 122.0, 117.4, 116.7, 114.6, 112.6, 60.9, 60.8, 50.7, 45.7, 27.4, 20.6, 13.9; exact mass calcd for $C_{19}H_{23}NO_4$: 329.1627, found 329.1634.

5-Butyl-5,6-dihydro-2,8,9-trimethoxy-7,10-phenanthridinediol (22b). The crude cyclobutenone **20b** in toluene (50 mL) was added dropwise to a refluxing toluene (150 mL) in 1 h 20 min under nitrogen, and the solution was refluxed for an additional 20 min. The solution was cooled to room temperature and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 2:1) gave **22b** (150 mg, 42% overall yield from **18b**) as a purple oil: IR ($CDCl_3$) 3520, 2942, 1611, 1573 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.96 (t, J = 7.3 Hz, 3H), 1.38 (sextet, J = 7.7 Hz, 2H), 1.67 (quintet, J = 7.7 Hz, 2H), 3.20 (t, J = 7.7 Hz, 2H), 3.81 (s, 3H), 3.91 (s, 3H), 3.94 (s, 3H), 4.11 (s, 2H), 5.42 (s, br, 1H), 5.95 (s, 1H), 6.73−6.80 (m, 2H), 8.05 (d, J = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 152.0, 140.7, 139.7, 138.2, 138.1, 137.0, 123.6, 117.2, 114.4, 113.5, 113.4, 111.2, 60.9, 60.8, 55.6, 51.1, 45.9, 27.5, 20.5, 13.9; exact mass calcd for $C_{20}H_{25}NO_5$: 359.1733, found 359.1723.

5-Allyl-5,6-dihydro-8,9-dimethoxy-7,10-phenanthridinediol (22c). In analogy to the above procedure, **22c** (157 mg, 63%) was obtained as a purple oil starting with **20c** (250 mg, 0.80 mmol): IR ($CDCl_3$) 3523, 1599 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.92 −3.95 (m, 8H), 4.16 (s, 2H), 5.26−5.35 (m, 2H), 5.36 (d, J = 1.47 Hz, 1H), 5.95 (s, 1H), 5.96−6.02 (m, 1H), 6.82 (d, J = 8.07 Hz, 1H), 6.87 (dt, J = 1.4, 8.07 Hz, 1H), 7.17 (dt, J = 1.4, 7.3 Hz, 1H), 8.38 (dd, J = 1.5, 7.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.1, 139.6, 138.3, 137.9, 136.9, 133.4, 128.4, 127.9, 122.3, 118.1, 117.9, 116.8, 114.5, 112.7, 60.9, 53.6, 45.7; exact mass calcd for $C_{18}H_{19}NO_4$: 313.1314, found 313.1328.

5-Allyl-5,6-dihydro-8-phenyl-9-methoxy-7,10-phenanthridinediol (22d). In analogy to the procedure used for the synthesis of **22b** the phenanthridinediol **22d** [138 mg, 48% overall yield from **18d** (150 mg, 0.8 mmol)] was obtained as a purple-brown oil: IR ($CDCl_3$) 3557, 3510, 1600 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.35 (s, 3H), 3.95 (d, J = 5.87 Hz, 2H), 4.22 (s, 2H), 4.77 (s, br, 1H), 5.28 (dd, J = 1.4, 10.2 Hz, 1H), 5.35 (dd, J = 1.8, 17.2 Hz, 1H), 5.99 (ddd, J = 1.8, 5.8, 10.6 Hz, 1H), 6.08 (s, 1H), 6.85 (d, J = 8.0 Hz, 1H), 6.89 (dt, J = 1.1, 7.7 Hz, 1H), 7.21 (dt, J = 1.4, 8.0 Hz, 1H), 7.44−7.48 (m, 3H), 7.53−7.55 (m, 2H), 8.47 (dd, J = 1.5, 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 146.6, 143.3, 140.5, 139.7, 133.3, 132.0, 130.2, 129.5, 128.8, 128.5, 128.4, 122.3, 119.4, 119.2, 118.0, 117.9, 117.7, 112.6, 60.7, 53.6, 46.0; exact mass calcd for $C_{23}H_{21}NO_3$: 359.1521, found 359.1510.

5-(*tert*-Butoxycarbonyl)-5,6-dihydro-8,9-dimethoxy-7,10-phenanthridinediol (22e). The solution of **20e** (460 mg, 1.23 mmol) in freshly distilled toluene (300 mL, 4.11×10^{-3} M) was refluxed under nitrogen for 3 h. The mixture was cooled to room temperature and the solvent removed *in vacuo*. The residue was dissolved in ethyl acetate (40 mL) and poured into a separatory funnel containing aqueous sodium dithionite solution (50 mL). The organic layer was dried and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 3:1) gave product **22e** (320 mg, 70%) as a light yellow solid: mp 196−198°; IR ($CDCl_3$) 3520,1691 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.49 (s, 9H), 3.94 (s, 3H), 3.95 (s, 3H), 4.77 (s, 2H), 5.51 (s, 1H), 5.97 (s, 1H), 7.18 (dt, J = 1.5, 7.7 Hz, 1H), 7.24 (dt, J = 1.5, 7.7 Hz, 1H), 7.54−7.56 (m, 1H), 8.35 (dd, J = 1.5, 7.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 140.0, 138.6, 137.6, 137.5, 127.9, 127.0, 126.7, 124.6, 124.2, 117.7, 114.2, 80.9, 60.9, 60.8, 40.6, 28.3; exact mass calcd for $C_{20}H_{23}NO_6$: 373.1525, found 373.1528.

5-(4-Pentenyl)-5,6-dihydro-8,9-dimethoxy-7,10-phenanthridinediol (22f). In analogy to the above procedure, **22f** (340 mg, 70%) was obtained as a purple oil starting with **20f** (489 mg, 1.43 mmol): IR ($CDCl_3$) 3522, 1637 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.81 (quintet, J = 7.3 Hz, 2H), 2.16 (hextet, J = 7.3 Hz, 2H), 3.3 (t, J = 7.7 Hz, 2H), 3.93 (s, 3H), 3.95 (s, 3H), 4.20 (s, 2H), 5.05 (dddd, J = 1.1, 1.5, 10.2, 17.2 Hz, 2H), 5.45 (s, br, 1H), 5.83−5.91 (m, 1H), 5.97 (s, br, 1H), 6.76 (d, J = 8.2 Hz, 1H), 6.84 (t, J = 7.5 Hz, 1H), 7.17 (dt, J = 1.4, 8.2 Hz, 1H), 8.37 (dd, J = 1.4, 7.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.1, 139.6, 138.2, 138.0, 137.9, 136.8, 128.5, 128.0, 122.1, 117.6, 116.7, 115.0, 114.5, 112.0, 60.8, 60.8, 50.3, 45.9, 31.3, 24.4; exact mass calcd for $C_{20}H_{23}NO_4$: 341.1627, found 341.1637.

5-(Anilinomethyl)-2,3-dimethoxy-1,4-benzenediol (25). In analogy to the above procedure, **25** (27 mg, 12%) was obtained as a light yellow oil from the thermolysis of **20c** (250 mg, 0.80 mmol): IR ($CDCl_3$) 3540 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.93 (s, 3H), 3.95 (s, 3H), 4.30 (s, 2H), 5.25 (s, 1H, OH), 6.48 (s, 1H, NH), 6.62 (s, 1H), 6.74 (d, J = 7.7 Hz, 2H), 6.78 (t, J = 7.3 Hz, 1H), 7.18−7.21 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 142.0, 141.6, 139.9, 138.9, 129.3, 119.9, 118.8, 114.2, 109.4, 61.1, 60.9, 45.1; exact mass calcd for $C_{15}H_{17}NO_4$: 275.1157, found 275.1171.

5-(tert-Butoxycarbonyl)-5,6-dihydro-8,9-dimethoxy-7,10-dioxophenanthridine (26). A mixture of **22e** (60 mg, 0.16 mmol), silver oxide (186 mg, 0.80 mmol), and potassium carbonate (110 mg, 0.80 mmol) in benzene (10 mL) was stirred at room temperature overnight. The mixture was filtered through a short silica gel plug and concentrated *in vacuo* to give product **26** (57 mg, 95%) as a red solid: mp 134−135 °C; IR ($CDCl_3$) 1698, 1650 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.50 (s, 9H), 4.03 (s, 3H), 4.06 (s, 3H), 4.65 (s, 2H), 7.19 (t, J = 7.3 Hz, 1H), 7.37 (t, J = 7.0 Hz, 1H), 7.60 (d, J = 8.4 Hz, 1H), 8.10 (dd, J = 8.1, 1.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.5, 181.5, 152.2, 144.7, 144.5, 139.5, 134.9, 132.3, 130.1, 129.1, 124.5, 124.4, 123.2, 82.0, 61.4, 61.2, 39.8, 28.2; exact mass calcd for $C_{20}H_{23}NO_6$ $(M + 2H)^+$: 373.1525, found 373.1538.

8,9-Dimethoxy-7,10-dioxophenanthridine (27). A mixture of **22c** (80 mg, 0.27 mmol), silver oxide (312 mg, 1.35 mmol), and potassium carbonate (186 mg, 1.347 mmol) in benzene (20 mL) was stirred at room temperature overnight. The mixture was filtered through a short silica gel plug and concentrated *in vacuo*. Chromatography (hexanes/EtOAc = 3:1) gave product **27** (43 mg, 60%) as a yellow solid: mp 90−91 °C; IR ($CDCl_3$) 1664, 1619 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.16 (s, 3H), 4.18 (s, 3H), 7.78 (t, J = 7.0 Hz, 1H), 7.87 (t, J = 7.0 Hz, 1H), 8.18 (dd, J = 0.7, 8.5 Hz, 1H), 9.39 (dd, J = 0.7, 8.5 Hz, 1H), 9.60 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 184.4, 182.3, 152.0, 147.7, 147.0, 145.2, 131.9, 131.0, 130.5, 130.3, 127.6, 122.0, 121.8, 61.5, 61.5; exact mass calcd for $C_{15}H_{11}NO_4$: 269.0688, found 269.0691.

2,3-Dimethoxy-5-methyl-1,4-benzoquinone (28). A degassed solution of **22a** (88 mg, 0.27 mmol) and potassium carbonate (158 mg, 1.07 mmol) in benzene (5 mL) was charged with nitrogen. To this was added silver oxide (266 mg, 1.07 mmol). The mixture was stirred for 10 min at room temperature, filtered through a short Celite plug, and concentrated *in vacuo*. Chromatography (hexanes/EtOAc = 3:1) gave product **27** (10 mg, 14%) and **28** (8 mg, 16%) both as yellow solid. **28**: mp 53−55 °C (lit.:[24] 57−58 °C)

(24) Sato, K.; Inoue, S.; Sato, H. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3455.

2,3-Dimethoxy-4-hydroxy-4-(3-carbazolyl-1-propynyl)-2-cyclobuten-1-one (30). To a solution of *N*-propargylcarbazole (472 mg, 2.3 mmol) in THF (15 mL) at −78 °C was added nBuLi (1.44 mL, 1.6 M in hexanes, 2.3 mmol). The solution was stirred for 20 min and then transferred to a solution of dimethyl squarate (326 mg, 2.3 mmol) in THF (20 mL) *via cannula*. The resulting solution was stirred for 35 min at −78 °C, quenched with saturated ammonium chloride (30 mL), and extracted with diethyl ether (2 × 15 mL). The combined organic portion was washed with brine (30 mL), dried over magnesium sulfate, and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 2:1) gave **30** (680 mg, 85%) as a light-brown solid: mp 99−100 °C; IR ($CDCl_3$) 3387, 1778, 1632 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.03 (s, 1H), 3.90 (s, 3H), 3.97 (s, 3H), 5.09 (s, 2H), 7.25−7.27 (m, 2H), 7.45−7.47 (m, 4H), 8.08 (d, J = 7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 179.8, 164.1, 139.8, 135.6, 125.9, 123.2, 120.4, 119.6, 108.7, 83.6, 78.4, 78.2, 60.0, 58.6, 32.6; exact mass calcd for $C_{21}H_{19}NO_4$ $(M + 2H)^+$: 349.1313, found 349.1312.

11,12-Dimethoxy-9*H*-indolo[3,2,1-*de*]phenanthridine-10,13-diol (31). A solution of **30** (80 mg, 0.23 mmol) in chlorobenzene (50 mL, N_2) was added dropwise to a refluxing chlorobenzene (100 mL) during a 1.5 h period, and the resulting solution was refluxed for an additional 15 min. The solution was cooled to room temperature and concentrated *in vacuo*. Chromatography (methylene chloride) gave product **31** (66 mg, 83%) as a light blue solid: mp 73−74 °C; IR ($CDCl_3$) 3521,1604, 1460 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.98 (s, 3H), 4.00 (s, 3H), 5.49 (s, 2H), 5.54 (s, 1H), 6.15 (s, 1H), 7.19 (t, J = 7.7 Hz, 1H), 7.26−7.29 (m, 1H), 7.48−7.50 (m, 2H), 7.89 (dd, J = 0.7, 7.7 Hz, 1H), 8.10 (d, J = 7.7 Hz, 1H), 8.50 (dd, J = 0.7, 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 141.3, 139.6, 138.8, 138.4, 138.1, 136.7, 125.2, 123.6, 123.4, 120.6, 120.5, 119.7, 119.5, 119.3, 116.6, 112.7, 112.5, 108.7, 60.9, 60.9, 41.0; exact mass calcd for $C_{21}H_{17}NO_4$: 347.1157, found 347.1153.

2,3-Dimethoxy-4-hydroxy-4-(3-indolyl-1-propynyl)-2-cyclobuten-1-one (33). To a solution of *N*-propargylindole (730 mg, 4.71 mmol) in THF (20 mL) at −78 °C was added nBuLi (2.94 mL, 1.6 M in hexanes, 4.71 mmol). The solution was stirred for 20 min and then transferred *via cannula* to a solution of dimethyl squarate (608 mg, 4.28 mmol) in THF (40 mL). The resulting solution was stirred for 35 min at −78 °C, quenched with saturated ammonium chloride (30 mL), and extracted with diethyl ether (2 × 15 mL). The combined organic portion was washed with brine (30 mL), dried over magnesium sulfate, and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 2:1) gave **33** (1.06 g, 83%) as a brown oil: IR (neat) 3381, 2247, 1778, 1641 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.90 (s, 1H), 3.91 (s, 3H), 4.07 (s, 3H), 4.90 (s, 2H), 6.50 (d, J = 2.6 Hz, 1H), 7.12 (t, J = 7.0 Hz, 1H), 7.15 (d, J = 3.3 Hz, 1H), 7.21−7.23 (m, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 180.3, 164.5, 135.7, 135.5, 128.7, 127.3, 121.8, 121.0, 119.8, 109.2, 102.0, 83.4, 79.3, 78.3, 60.1, 58.6, 36.0; exact mass calcd for $C_{17}H_{15}NO_4$: 297.1001, found 297.1009.

8,9-Dimethoxy-5,6-dihydroisoindoloindole-7,10-diol (34). A solution of **33** (110 mg, 0.37 mmol) in chlorobenzene (50 mL) was added dropwise to a refluxing chlorobenzene (250 mL, N_2) during a period of 1.5 h, and the solution was refluxed for an additional 20 min. The solution was cooled to room temperature and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 2:1) gave product **34** (63 mg, 57%) as a green-yellowish solid: mp 160 °C dec; IR ($CDCl_3$) 3539 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.96 (s, 3H), 3.97 (s, 3H), 5.03 (s, 2H), 5.47 (s, 1H), 5.63 (s, 1H), 6.63 (s, 1H), 7.08 (t, J = 7.1 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.65 (d, J = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 141.6, 139.6, 139.1, 137.8, 137.1, 133.8, 133.0, 121.7, 121.5, 121.2, 119.2, 115.3, 108.9, 93.0, 61.1, 61.0, 46.2; exact mass calcd for $C_{17}H_{15}NO_4$: 297.1001, found 297.0987.

9,10-Dimethoxy-6,7-dihydropyrrolophenanthridine-8,11-diol (35). In analogy to the above procedure, product **35** (13 mg, 12%) was obtained as a blue oil starting with **33** (110 mg, 0.37 mmol): IR ($CDCl_3$) 3532 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.96 (s, 3H), 3.97 (s, 3H), 5.44 (s, 1H), 5.46 (s, 2H), 6.08 (s, 1H), 6.52 (d, J = 2.9 Hz, 1H), 7.07 (t, J = 7.7 Hz, 1H), 7.12 (d, J = 3.3 Hz, 1H), 7.44 (d, J = 7.7 Hz, 1H), 8.20 (d, J = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 141.3, 138.6, 138.2, 138.0, 132.9, 125.4, 120.4, 120.0, 119.6, 117.2, 112.7, 112.6, 102.3, 60.9, 60.8, 43.2; exact mass calcd for $C_{17}H_{15}NO_4$: 297.1001, found 297.1012.

2,3-Dimethoxy-5-(indolylmethyl)-1,4-benzenediol (36). In analogy to the above procedure, product **36** (9 mg, 8%) was obtained as a brown oil starting with **33** (110 mg, 0.37 mmol): IR (neat) 3538, 2945, 1611 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.87 (s, 3H), 3.92 (s, 3H), 5.28 (s, 2H), 5.38 (s, br, 1H), 5.63 (s, br, 1H), 6.27 (s, 1H), 6.54 (d, J = 2.9 Hz, 1H), 7.12 (t, J = 7.7 Hz, 1H), 7.20−7.22 (m, 2H), 7.43 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.0, 139.8, 139.1, 138.6, 136.0, 128.4, 128.3, 121.3, 120.7, 119.2, 118.9, 109.6, 109.2, 101.1, 60.7, 60.6, 44.2; exact mass calcd for $C_{17}H_{17}NO_4$: 299.1157, found 299.1170.

2,3-Dimethoxy-4-hydroxy-4-[3-[*N*-methyl-*N*-(1-naphthyl)amino]-1-propynyl]-2-cyclobuten-1-one (38). To a solution of *N*-methyl-*N*-propargyl-1-aminonaphthalene (552 mg, 2.83 mmol) in THF (15 mL) at −78 °C was added nBuLi (2.02 mL, 1.4 M in hexanes, 2.83 mmol), and the resulting reaction mixture was stirred for 25 min. It was then transferred to a solution of dimethyl squarate (402 mg, 2.83 mmol) in THF (30 mL) *via cannula*. The resulting mixture was stirred for 30 min at −78 °C, quenched with saturated ammonium chloride (30 mL), and extracted with diethyl ether (2 × 15 mL). The combined organic portion was washed with brine (30 mL), dried over magnesium sulfate, and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 1:1) gave **38** (829 mg, 87%) as a viscous yellow oil: IR (neat) 3384, 1780, 1635 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.97 (s, 3H), 3.93 (s, 3H), 4.01 (s, 2H), 4.08 (s, 3H), 4.36 (s, 1H), 7.21 (dd, J = 0.8, 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.47−7.54 (m, 2H), 7.57 (d, J = 8.0 Hz, 1H), 7.82−7.84 (m, 1H), 8.18 (dd, J = 0.8, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 181.0, 164.9, 147.7, 135.1, 134.6, 128.7, 125.7, 125.5, 125.4, 123.9, 123.4, 116.5, 85.2, 79.8, 78.2, 59.8, 58.4, 46.8, 40.8; exact mass calcd for $C_{20}H_{19}NO_4$: 337.1314, found 337.1315.

10,11-Dimethoxy-*N*-methyl-7,8-dihydrobenzophenanthridine-9,12-diol (39). A solution of **38** (150 mg, 0.455 mmol) in chlorobenzene (25 mL, N_2) was added dropwise to refluxing chlorobenzene (125 mL) during a period of 1.5 h. The reaction solution was refluxed for an additional 20 min, cooled to room temperature, and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 3:1) gave **39** (102 mg, 68%) as a light purple solid: mp 50−52 °C; IR (neat) 3503 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.70 (s, 3H), 3.98 (s, 3H), 4.00 (s, 3H), 4.27 (s, 2H), 5.46 (s, 1H), 6.04 (s, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 7.1 Hz, 1H), 7.67 (d, J = 8.7 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 8.40 (d, J = 8.3 Hz, 1H), 8.55 (d, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.0, 139.7, 138.7, 138.2, 133.5, 129.2, 127.8, 126.1, 125.6, 125.5, 124.3, 123.9, 123.5, 115.0, 114.4, 60.8, 60.8, 48.1, 41.1; exact mass calcd for $C_{20}H_{19}NO_4$: 337.1314, found 337.1314.

2,3-Dimethoxy-4-hydroxy-4-(3-indolinyl-1-propynyl)-2-cyclobuten-1-one (42). To a solution of *N*-propargylindoline (3.03 g, 19.3 mmol) in THF (60 mL) at −78 °C was added nBuLi (12.1 mL, 1.6 M in hexanes, 19.3 mmol), and the mixture was stirred for 25 min. It was transferred to a solution of dimethyl squarate (2.50 g, 17.6 mmol) in THF (90 mL) *via cannula*. The resulting solution was stirred for 35 min at −78 °C, quenched with saturated ammonium chloride (50 mL), and extracted with ethyl acetate (2 × 35 mL). The combined organic portion was washed with brine (40 mL), dried over magnesium sulfate, and concentrated *in vacuo*. Chromatography (hexanes/ethyl acetate = 2:1) gave **42** (4.60 g, 87%) as a yellow solid: mp 104−105 °C; IR ($CDCl_3$) 3380, 1781, 1647 cm^{-1}, ^1H NMR ($CDCl_3$, 300 MHz) δ 2.95 (t, J = 8.1 Hz, 2H), 3.37 (dt, J = 2.2, 8.1 Hz, 2H), 3.61−3.62 (m, 1H), 3.92 (s, 3H), 3.97 (s, 2H), 3.98 (s, 3H), 6.56 (d, J = 7.7 Hz, 1H), 6.73 (dt, J = 0.9, 7.7 Hz, 1H), 7.07−7.10 (m, 2H); ^{13}C NMR

(25) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

($CDCl_3$, 125 MHz) δ 180.4, 164.6, 150.7, 135.4, 130.7, 127.1, 124.4, 119.0, 108.5, 84.7, 78.5, 78.3, 59.7, 58.5, 53.1, 38.6, 28.4; exact mass calcd for $C_{17}H_{18}NO_4$ $(MH)^+$: 300.1235, found 300.1230.

9,10-Dimethoxy-4,5,6,7-tetrahydropyrrolophenanthridine-8,11-diol (43). A solution of **42** (250 mg, 0.84 mmol) in *p*-xylene (150 mL) was added dropwise to a refluxing *p*-xylene solution (200 mL, N_2) during a 1 h and 45 min period, and the mixture was refluxed for an additional 5 min. The solution was cooled to room temperature and concentrated *in vacuo*. Chromatography (methylene chloride/ethyl acetate = 20:1) gave product **43** (100 mg, 40%) as a purple solid: mp 130−132 °C; IR ($CDCl_3$) 3527 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.00 (t, J = 8.1 Hz, 2H), 3.31 (t, J = 8.1 Hz, 2H), 3.88 (s, 6H), 4.10 (s, 2H), 5.56 (s, 1H), 5.97 (s, 1H), 6.76 (t, J = 7.4 Hz, 1H), 7.00 (dt, J = 0.7, 7.3 Hz, 1H), 8.06 (d, J = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 149.8, 140.1, 138.3, 138.1, 138.0, 128.0, 125.2, 123.3, 119.3, 117.8, 114.8, 113.8, 60.8, 60.7, 55.4, 46.8, 29.0; exact mass calcd for $C_{17}H_{17}NO_4$: 299.1157, found 299.1149.

In addition to **43**, the hydroquinone **36** (125 mg 50%) was also isolated from the chromatographic purification step. The spectral data obtained for this compound were shown to be identical to those realized from the minor (8%) product obtained in the thermolysis of **33**.

9,10-Dimethoxy-4,5,6,7-tetrahydro-8,11-bis[diethoxyphosphinyl)oxy]pyrrolophenanthridine (44). Sodium hydride (313 mg, 50% in oil suspension, 6.52 mmol) was washed with pentane (2 × 10 mL) and covered with THF (10 mL). To the cooled (0 °C) solution of sodium hydride was added a solution of **43** (650 mg, 2.17 mmol) in THF (20 mL). The mixture was stirred at room temperature for 3 h, cooled to 0 °C, and diethyl chlorophosphonate (1.13 g, 6.52 mmol) was added. The resulting solution was stirred at room temperature overnight and then washed with saturated aqueous sodium bicarbonate (40 mL). The aqueous layer was extracted with ethyl acetate (3 × 30 mL), the combined organic layer was washed with brine, dried over magnesium sulfate, and concentrated *in vacuo*. Chromatography (chloroform/methanol = 30:1) gave product **44** (890 mg, 72%) as a red oil: IR (neat) 1632, 1426, 1280, 1084 cm^{-1}, ^1H NMR ($CDCl_3$, 500 MHz) δ 1.24 (t, J = 5.9 Hz, 6H), 1.34(t, J = 5.9 Hz, 6H), 3.00 (t, J = 8.1 Hz, 2H), 3.28 (t, J = 8.1 Hz, 2H), 3.95 (s, 3H), 3.96 (s, 3H), 4.02−4.14 (m, 6H), 4.20−4.25 (m, 4H), 6.74 (t, J = 7.3 Hz, 1H), 7.00 (dt, J = 0.9, 7.3 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.9, 145.0, 144.3, 139.3, 137.9, 128.3, 125.2, 124.2, 122.3, 120.4, 119.3, 116.2, 64.6, 64.5, 64.3, 64.3, 61.0, 55.4, 47.9, 28.8, 16.0, 16.0, 15.9, 15.8; exact mass calcd for $C_{25}H_{35}NO_{10}P_2$: 571.1736, found 571.1734.

Assoanine (40). Ammonia was condensed in a three-neck round-bottom flask (500 mL) under nitrogen at −78 °C; the flask was provided with a cold-finger condenser containing dry ice and acetone. Compound **44** (270 mg, 0.47 mmol) in dry ether (18 mL) was added followed by sodium (76 mg, 3.3 mmol) in small pieces. The mixture was stirred at −78 °C for 1 h and then stirred at room temperature overnight to allow ammonia to evaporate. The reaction was quenched with methanol (20 mL) and saturated ammonium chloride (30 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layer was dried over magnesium sulfate, and concentrated *in vacuo*. Chromatography (hexanes/EtOAc = 4:1) gave assoanine (**40**) (31 mg, 25%) as a light brown solid: mp 166−168 °C (lit.,[18] mp 175−176 °C). The ^1H NMR and ^{13}C NMR data observed for this product are identical to those reported in the literature for the natural product.[17,18]

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Supporting Information Available: ^{13}C NMR spectra of compounds **10a**−**c**, **11**, **12a**,**b**, **17a**−**f**, 1**9a-f**, **20a**, **20c**, **20e**, **20f**, **22a**−**f**, **25**−**27**, **31**, **33**−**36**, **38**, **39**, and **42**−**45** (43 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS: see any current masthead page for ordering information.

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